Remarks

Claims 1, 2, 8, 11, 15, 16, 18, 19, 21-35, 37, 42, 43, 45,-47, 50, 52-54, 56, 60, 62, 68, 70, 76, 77 and 83 are pending in the application and are subject to a restriction requirement. In the present response new claims 84-89 are added.

Explanation of the Amendments

The amendments to the specification were entered to correct typographical errors that were noted which are mostly obvious typographical errors. On page 100 and page 109, the K562 cell line was erroneously characterized as a non-small cell lung carcinoma cell line. This has now been corrected to chronic myelogenous leukemia. Since the K562 cell line is well known by the person skilled in the art as a chronic myelogenous leukemia cell line (*see, e.g.,* E. Klein, *et al.*, "Properties of the K562 cell line, derived from a patient with chronic myeloid leukemia" *Int. J. Cancer.*, **1976**, *18*(4), 421-31), the reference to the K562 in the original specification would be understood by the person in the art to be a chronic myelogenous leukemia cell line.

Claims 1 and 2 have been amended by the deletion of b=1.

Claim 15 has been amended by the deletion of n=1 (corresponding to the deletion of b=1 in claim 1). The phrase "wherein the sum of n is selected from" has also been reworded to "with the proviso that the sum of the values of n is selected from" to improve clarity.

In claim 18, the superfluous definition of "n is 0 or 1" has been deleted.

In claim 19, the superfluous definition of "n is 0 or 1" has been deleted, and n is included in the list of substituents designated as being as defined in claim 18.

Claim 22 is amended to correct a spelling error ((*E*)-*N*-(3-hydroxy-4-methoxyphenyl)-3-(2,4,6-trimethoxyphenyl)-2-propenamide).

Claim 23 has been amended to correct a punctuation error.

Claims 43, 50, 53, 62, 68, and 76 have been amended to conform the scope of compounds used in the claimed method to the compounds according to claim 1.

Claim 45 has been amended to correct typographical errors.

Claim 62 has been amended for clarity by the amendment of "the bone marrow" to "the removed bone marrow".

Claims 84-89 correspond to the pre-amendment subject matter of claims 43, 50, 53, 62, 68, and 76.

Response to the Restriction Requirement

The examiner has required restriction between Groups I, II and III, characterized by the examiner as:

> **Group I**, claim(s) 1-2, 8, 11, 15-16, 18-19, 21-23, 24-35, 43, 45-47, 50, 54, 56, 60, 62, 68, 70, and 76-77 drawn to compounds, composition, process of preparing and method of treatment when they are non heterocyclic.
>
> **Group II**, claim(s) 1-2; 8, 11, 15-1 6, 18-19, 21-23, 24-35, 43, 45-47, 50, 54, 56, 60, 62, 68, 70, and 76-77 drawn to compounds, composition, process of preparing and method of treatment when they are heterocyclic.
>
> **Group III**, claim(s) 37, 42, 53 drawn to conjugate and composition and method of treatment.

Since it was not clear to the applicants to which moiety in the compounds of formula I to which "*they* are not heterocyclic" (or "*they* are heterocyclic") referred, a telephone call was made to the examiner on December 22, 2006. The examiner clarified that the characterization "heterocyclic" (or not) was to be understood as referring to rings A and B. Therefore the applicants' understanding is that the restriction requirement divides the claims into the groups that may be defined as follows:

> **Group I:** Compounds, compositions, process of preparing and methods of treatment wherein, in the compounds, both ring A and ring B are aryl (i.e. neither ring is heteroaryl);
>
> **Group II:** Compounds, compositions, process of preparing and methods of treatment wherein, in the compounds, either ring A or ring B is heteroaryl, or both rings A and B are heteroaryl (i.e. either ring is heteroaryl);

Group III: As defined above.

The applicants respectfully point out that given the interpretation, the examiner does not appear to have correctly identified the claims that read on Groups I and II. In the applicants' view, the claims among which restriction has been required that read on each Group are as follows:

Group I: Claims 1, 2, 8, 11, 15, 16, 18, 19, 21-35, 43, 45-47, 50, 52, 54, 56, 60, 62, 68, 70, 76, 77 and 83-89.

Group II: Claims 1, 2, 8, 24-26, 35, 43, 45-47, 50, 52, 54, 56, 60, 62, 68, 70, 76, 77, and 84-89.

Group III: Claims 37, 42, and 53.

The applicants' listing for Group I differs from the examiner's listing by the addition of claims 52 and 83. These claims were missing from the examiner's listing of pending claims and are assumed to have been inadvertently omitted.

The applicants' listing for Group II differs from the examiner's listing because rings A and B are both limited to phenyl (and therefore cannot be heteroaryl) in the definitions of claims 11, 15, 16, 18, 19, 21, 23, 27-34 and 83. In addition, in each of the species in claim 22, rings A and B are phenyl.

In new claims 84 to 89, rings A and B may be either aryl or heteroaryl, and therefore these claims have been included in Groups I and II in applicants' listing.

Subject to the interpretation set forth above, the applicants **elect Group I, but respectfully traverse the restriction requirement**. If the applicants' interpretation of the restriction requirement, as set forth above is incorrect, the examiner is respectfully requested to issue a new office action more clearly defining the groups among which restriction is being required. The **elected species is (*E*)-*N*-(3-hydroxy-4-methoxyphenyl)-3-(2,4,6-trimethoxy-phenyl)-2-propenamide** (i.e. the structure listed as example 11 in Table 5 (p. 101 of the specification)). Claims 1, 2, 8, 22 read on a compound of the elected species. In addition, claims 24 and 25 read on processes of preparing the elected species. Claim 35 reads on pharmaceutical compositions comprising a compound of the elected species. Claims 43, 45, 46, 47, 50, 52, 54,

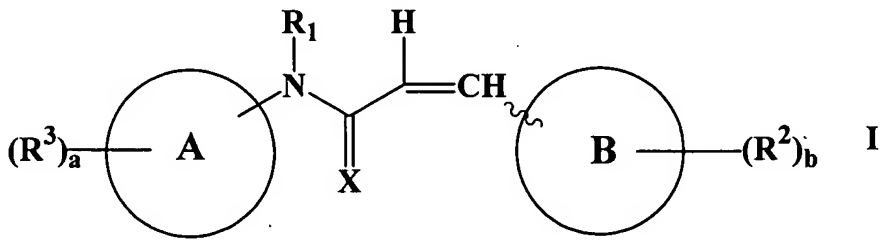
56, 60, 62, 68, 70, 76, 77, and 84-89 read on methods of treatment using a compound of the elected species.

The examiner states that unity is lacking because the Groups I-III do not relate to a single general inventive concept under PCT Rule 13.1 because they allegedly lack the same or corresponding special technical features. The examiner states that the reason that Groups I and Groups II lack the same or corresponding technical feature is that Group I compounds are non-heterocyclic whereas group II are heterocyclic. The examiner states that "likewise" Group III lacks the same or corresponding technical feature because it is "drawn to [a] conjugate as against compounds of Groups I and II".

MPEP 1893.03(d) reminds examiners that "unity of invention (not restriction) practice is applicable in ... national stage applications submitted under 35 U.S.C. 371." Under the decision in *Caterpillar Tractor Co. v. Com'r Pat. & Trademarks*, 650 F.Supp. 218 (E.D. Va. 1986), unity of invention must be determined under the provisions of the P.C.T. in a national stage application filed under 35 U.S.C. § 371. Therefore the examiner must make any restriction requirement in accordance with the P.C.T. the P.C.T. rules (specifically Rule 13) and the Administrative Instructions under the P.C.T.

For unity of invention, P.C.T. Rule 13.2 requires "a technical relationship among th[e] inventions involving *one or more* of the same or corresponding special technical features." (emphasis added). The WIPO Preliminary Examination Guidelines on Markush practice in the determination of unity of invention point out, "the fact that the alternatives of a Markush group *can* be differently classified is not, taken alone, considered to be justification for a finding of lack of unity of invention". P.C.T. International Search and Preliminary Examination Guidelines, 10.17(d) (March 25, 2004) (emphasis added).

A common special technical feature linking the Groups is the novel compound of Formula I (defined in claim 1):



I

The compounds of Formula I are clearly a unifying technical feature of Groups I and II. The examiner does not appear to allege otherwise other than by drawing a distinction between "aryl" and "heteroaryl" in the definitions of the rings A and B to conclude that unity of invention is lacking as between compounds where A and B are both aryl (Group I), and those wherein either A or B, or both, are heteroaryl (Group II). Both Groups I and II are, however, drawn to compounds of Formula I, and compositions containing, processes of preparing, and methods of treatment using the compounds. The compounds of Formula I are therefore a unifying technical feature of Groups I and II.

The fact that options within the definitions of A and B the options can be differently classified as aryl or heteroaryl does not defeat unity of invention. Aryl and heteroaryl rings, although capable of being differently classified, nevertheless belong to a recognized class, namely aromatic rings. The art recognizes aromatic rings as a single class which includes both carbocyclic and heterocyclic rings, and is defined as encompassing conjugated unsaturated ring systems with 4n+2 pi electrons. As the WIPO guidelines point out, the possibility that the alternatives of a Markush group *can* be differently classified is not sufficient justification for a finding of lack of unity of invention.

The Formula I structure is also a special technical feature linking Groups I and II with Group III. The structure of the claimed antibody conjugates comprise the structure of Formula I linked to an antibody. The claims to the antibody conjugate are clearly part of the same general inventive concept as the claims to the compounds and their medical use. The inventors have invented the novel compound of Formula I and its therapeutic utility. The antibody conjugates connect the compound of Formula I to an antibody in order to target the delivery of the compound of Formula I to the appropriate site in the body, but, nevertheless, the useful therapeutic utility of the conjugate arises because of the incorporation of Formula I as an essential structural element which imparts the desired activity. The Formula I structure is therefore a technical feature unifying Group III with Groups I and II.

It is respectfully pointed out that the examiner's method of analyzing unity of invention cannot properly determine whether there is unity of the invention because the examiner appears to focus on differences between the Groups, and whether they can be differently classified. The examiner concludes that the Groups lack the same or corresponding technical feature because of

differences between the groups. The WIPO guidelines clearly explain that the possibility of different classification is not sufficient justification for a finding of lack of unity of invention. Further, differences, between the groups, taken alone, are insufficient demonstrate that the inventions lack *a* common special technical feature - the differnce only show that *the particular* feature defining the difference is not a technical feature common to the groups. Such differences do not preclude *another* technical feature from being a common technical feature linking the Groups.

The examiner's statement that "should applicant traverse on the ground that the inventions or species rare not patentably distinct, applicant should submit evidence ... showing the inventions or species to be obvious variants or clearly admit on the record that this is the case" is inapplicable to applicants' traversal on the grounds that unity of invention is not lacking. While patentable distinctness may be relevant in traversing a restriction requirement under U.S. restriction practice, unity of invention and not restriction practice is applicable in national stage applications submitted under 35 U.S.C. § 371. Applicants therefore take no position in the present response as to whether the Groups identified by the examiner are, or are not, obvious variants.

In view of the foregoing, it is respectfully submitted that unity of invention clearly exists as between Groups I, II, and III, and that the restriction requirement is improper. The examiner is therefore respectfully requested to reconsider and withdraw the restriction requirement.

Respectfully submitted,

M.V. Ramana REDDY, *et al.*

BY _____

DANIEL A. MONACO
Registration No. 30,480
Drinker Biddle & Reath LLP
One Logan Square
18th and Cherry Streets
Philadelphia, PA 19103-6996
Tel: (215) 988-3312
Fax: (215) 988-2757
Attorney for Applicants